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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,373	09/28/2001	Patrick J. Muraca	5568/1042	3910

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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 01/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,373	MURACA, PATRICK J.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,9,10,12-15 and 17-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,9,10 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *17-38* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission, filed 11/2/04 and 9/28/04, have been entered.

Amended claims 1-2, 9-10, and 12-15 and cancelled claims 3-8, 11, and 16, filed 11/2/04, are acknowledged.

Claims herein under examination are 1-2, 9-10, and 12-15.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 10, 12-13, and 15 are rejected under 35 U.S.C. 102(e)(2) as being anticipated by Lincoln et al. (P/N 6,553,317).

Lincoln et al. disclose the use of bioinformatics to study genes differentially expressed or commonly expressed in different tissues or cell lines, such as normal (normally proliferating cells) and cancerous tissue (abnormally proliferating cells) (col. 1, lines 46-48). Lincoln et al. disclose using a microarray with multiple samples (col. 3, lines 10-12) which represents first and second locations for placement of a test tissue and microarray, as stated in instant claim 1. Lincoln et al. disclose processing clones in groups on a 96-well plastic culture dish with each chamber/well comprising an indentation in the dish to separate samples (col. 12, lines 20-25) which represents a stably associated samples with a distinct, known sublocation on a substrate, as stated in instant claim 1. Lincoln et al. disclose a barcode (identifier) for a lot or 96-well plate whose value is placed in a barcode field of a table in a database (col. 21, lines 30-41) which represents a substrate with an identifier that provides access to a database, as stated in instant claim 1. The samples in a plastic culture dish represent the sample (tissue or cells) being plastic-embedded, as stated in instant claim 10. The information on the plastic culture dish, including precise sample location with lot and well information, is recorded for each sample and given to customers (col. 12, lines 29-36). Lincoln et al. disclose using a relational database system for storing biomolecular sequence information with biological annotations (col. 2, lines 14-20) including information identifying (identifiers) sequences (col. 2, lines 28-34). Lincoln et al. disclose a system allowing a user to selectively view information regarding sequences and reagent specifications (col. 2, lines 34-37) including a graphical user interface where a query is entered and matches between query and information is displayed (col. 2, lines 46-50). Lincoln et al. disclose using a relational database with tables (col. 15, lines 44-49) including a library table that includes records of each library in the gene expression database including an identifier

(LibraryID) (col. 16, lines 7-9). Lincoln et al. disclose the library table as having a "TissueID" attribute that is inherited from a "TissueSpecimen" table) and a "Tissue_Category" attribute as well as a "Lib_Description" attribute including information such as tissue name, disease state, patient age/gender (col. 16, lines 6-32). Lincoln et al. disclose providing further information about a donor in a "MedicalHistory" table including information such as a problem such as breast cancer, breast, and neoplasm (col. 20, lines 33-40). Lincoln et al. disclose using a network to which the network server and clients are connected (col. 13, lines 3-9). Lincoln et al. disclose entries in various results screens may provide links to other information in the database (col. 23, lines 10-13) as stated in instant claim 2. Lincoln et al. disclose each tissue specimen (as uniquely identified by TissueID) may have several diagnoses (i.e. normal, diseased, involved, cancerous) and each donor may provide multiple tissue specimens (col. 19, lines 35-67) which represent a progression of cancer from an early stage (i.e. normal) to an advanced stage (i.e. cancerous), as stated in instant claim 1. This act of providing multiple tissue specimens that are "cancerous" or "involved" is reasonably interpreted to include specimens from sites of a secondary metastasis of cancer. Lincoln et al. disclose different development stages (col. 20, lines 13-14). Lincoln et al. disclose studying or monitoring drug resistance in certain tissue (col. 5, lines 1-3) which represents substantially homogeneous cells (as stated in instant claim 13) and samples from patients treated with a drug (as stated in instant claim 15). Lincoln et al. disclose obtaining clones from a particular tissue (col. 4, lines 42-44) and using a set of clones on a microarray (col. 3, lines 10-12) which represents a microarray associated with tissue-material. The clones are a part of the tissue, such that they represent a test tissue. Therefore, placing them in a location on a microarray represents a first location placement of a test tissue. Instant claim 1 states the profile

array substrate "allows testing" and "comparison" but does not state that the testing and comparison are actually done on the profile array substrate itself. Lincoln et al. disclose a given clone being compared contemporaneously, in parallel, against other clones in the internal and public databases (col. 5, line 65 to col. 6, line 4) which represents a simultaneous testing allowing for side-by-side comparisons of the "test tissue" with the samples in the control, as stated in instant claim 1. Lincoln et al. disclose comparing new sequences against existing (known) clone sequences to classify new clones as belonging to a known sequence already provided in the internal database (col. 7, lines 38-53). It is further noted that the phrases "for placement" on lines 2 and 3 as well as the phrase "wherein the profile array substrate allows testing... in the control oncology tissue microarray" in instant claim 1 are all intended uses which carry no patentable weight as to the article of manufacture being claimed.

Thus, Lincoln et al. anticipate the limitations in claims 1, 2, 10, 12-13, and 15.

Applicant states the microarray comprises samples representing the progression of a type of cancer from an early stage to an advanced stage. Applicant states a control tissue microarray allows for a side-by-side comparison of an unknown test tissue with various known samples of the microarray. Applicant states these featured amendments distinguish the claimed invention from the cited art. This is found unpersuasive as the comprising limitation of the microarray only mentions samples representing a progression of early to advanced stage cancer which is disclosed in the Lincoln et al. reference as the instantly claimed samples can be any type of sample, such as tissue, cells, or DNA. The side-by-side comparison allowance is an intended use that can actually take place with database comparison, as already disclosed by Lincoln et al.

Applicant states instant claim 1 has been amended to clarify first and second locations. This statement is found unpersuasive as these limitations include intended use phrases "for placement..." which carry no patentable weight in these article of manufacture claims.

Applicant states the Lincoln et al. reference does not disclose a tissue microarray and does not disclose any type of control oncology tissue microarray comprising normal tissue and samples representing a progression of a type of cancer. This is found unpersuasive as the comprising limitation of the microarray only mentions samples representing a progression of early to advanced stage cancer which is disclosed in the Lincoln et al. reference as the instantly claimed samples can be any type of sample, such as tissue, cells, or DNA. It is noted that only the structural limitations found in the instant claims must be anticipated by the prior art reference. Because the Lincoln et al. reference discloses all of the structural limitations in instant claims 1-2, 9-10, and 12-15, this prior art reference anticipates these claims.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 9-10, and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lincoln et al. (P/N 6,553,317) in view of Schraml et al. (Clinical Cancer Research, August

1999, vol. 5, pages 1966-1975) and Lehman et al. (Cancer Research, February 2000, vol. 60, pages 1062-1069).

Lincoln et al. describe the use of bioinformatics to study genes differentially expressed or commonly expressed in different tissues or cell lines, such as normal (normally proliferating cells) and cancerous tissue (abnormally proliferating cells) (col. 1, lines 46-48). Lincoln et al. describe using a microarray with multiple samples (col. 3, lines 10-12) which represents first and second locations for placement of a test tissue and microarray, as stated in instant claim 1. Lincoln et al. describe processing clones in groups on a 96-well plastic culture dish with each chamber/well comprising an indentation in the dish to separate samples (col. 12, lines 20-25) which represents a stably associated samples with a distinct, known sublocation on a substrate, as stated in instant claim 1. Lincoln et al. describe a barcode (identifier) for a lot or 96-well plate whose value is placed in a barcode field of a table in a database (col. 21, lines 30-41) which represents a substrate with an identifier that provides access to a database, as stated in instant claim 1. The samples in a plastic culture dish represent the sample (tissue or cells) being plastic-embedded, as stated in instant claim 10. The information on the plastic culture dish, including precise sample location with lot and well information, is recorded for each sample and given to customers (col. 12, lines 29-36). Lincoln et al. describe using a relational database system for storing biomolecular sequence information with biological annotations (col. 2, lines 14-20) including information identifying (identifiers) sequences (col. 2, lines 28-34). Lincoln et al. describe a system allowing a user to selectively view information regarding sequences and reagent specifications (col. 2, lines 34-37) including a graphical user interface where a query is entered and matches between query and information is displayed (col. 2, lines 46-50). Lincoln et

al. describe using a relational database with tables (col. 15, lines 44-49) including a library table that includes records of each library in the gene expression database including an identifier (LibraryID) (col. 16, lines 7-9). Lincoln et al. describe the library table as having a "TissueID" attribute that is inherited from a "TissueSpecimen" table) and a "Tissue_Category" attribute as well as a "Lib_Description" attribute including information such as tissue name, disease state, patient age/gender (col. 16, lines 6-32). Lincoln et al. describe providing further information about a donor in a "MedicalHistory" table including information such as a problem such as breast cancer, breast, and neoplasm (col. 20, lines 33-40). Lincoln et al. describe using a network to which the network server and clients are connected (col. 13, lines 3-9). Lincoln et al. describe entries in various results screens may provide links to other information in the database (col. 23, lines 10-13) as stated in instant claim 2. Lincoln et al. describe each tissue specimen (as uniquely identified by TissueID) may have several diagnoses (i.e. normal, diseased, involved, cancerous) and each donor may provide multiple tissue specimens (col. 19, lines 35-67) which represent a progression of cancer from an early stage (i.e. normal) to an advanced stage (i.e. cancerous), as stated in instant claim 1. This act of providing multiple tissue specimens that are "cancerous" or "involved" is reasonably interpreted to include specimens from sites of a secondary metastasis of cancer. Lincoln et al. describe different development stages (col. 20, lines 13-14). Lincoln et al. describe studying or monitoring drug resistance in certain tissue (col. 5, lines 1-3) which represents substantially homogeneous cells (as stated in instant claim 13) and samples from patients treated with a drug (as stated in instant claim 15). Lincoln et al. describe obtaining clones from a particular tissue (col. 4, lines 42-44) and using a set of clones on a microarray (col. 3, lines 10-12) which represents a microarray associated with tissue-material.

The clones are a part of the tissue, such that they represent a test tissue. Therefore, placing them in a location on a microarray represents a first location placement of a test tissue. Instant claim 1 states the profile array substrate "allows testing" and "comparison" but does not state that the testing and comparison are actually done on the profile array substrate itself. Lincoln et al. describe a given clone being compared contemporaneously, in parallel, against other clones in the internal and public databases (col. 5, line 65 to col. 6, line 4) which represents a simultaneous testing allowing for side-by-side comparisons of the "test tissue" with the samples in the control, as stated in instant claim 1. Lincoln et al. describe comparing new sequences against existing (known) clone sequences to classify new clones as belonging to a known sequence already provided in the internal database (col. 7, lines 38-53). It is further noted that the phrases "for placement" on lines 2 and 3 as well as the phrase "wherein the profile array substrate allows testing... in the control oncology tissue microarray" in instant claim 1 are all intended uses which carry no patentable weight as to the article of manufacture being claimed. However, Lincoln et al. do not describe using samples greater than about 0.6 mm in diameter, and cancer-specific markers.

Schraml et al. describe using tissue microarrays for gene amplification surveys in many different tissue types (title). Schraml et al. describe using a tissue microarray consisting of samples from 17 different tumor types with 397 individual tumors arrayed in a single paraffin block (representing at least about 10% of the samples of the microarray, (diameter, 0.6mm) (abstract and Figure 1) which is greater than about 0.6 mm in diameter, as stated in instant claim 9. Schraml et al. describe finding gene markers (i.e. CCND1) amplified in breast and other cancerous tissue types (abstract and page 1966, col. 2, first paragraph), as stated in instant claim

14. Schraml et al. describe hundreds of samples are precisely arrayed in a new paraffin block (page 1966, col. 2, second paragraph) which represents stably associated samples with distinct, known sublocations on a substrate, as stated in instant claim 1. Schraml et al. describe the precise positioning of tissue specimens to enable the generation of multiple replicate array blocks, each having samples from the same tissue specimens at identical coordinates (page 1970, col. 2), as stated in instant claim 1. Schraml et al. describe using frozen tissue samples from primary tumors (abnormally proliferating cells) and normal tissues (normally proliferating cells) and embedding the specimens in paraffin (page 1966, col. 2, third paragraph), as stated in instant claim 10. Schraml et al. describe using tumors in different stages and grades, including 96 breast tumors (page 1967, col. 1, second paragraph), as stated in instant claim 12.

Lehman et al. describe studying breast cancer patients for activity of exon and intron base changes in the p53 gene (abstract). Lehman et al. describe patient information, such as age (abstract). Lehman et al. describe gene studies in response to drug treatment (abstract). In Table 1, Lehman et al. describe various statistics of patients including the stage of breast cancer. Lehman et al. describe coding the samples from patients and entering the information into a database (page 1063, col. 1, first paragraph). Lehman et al. describe collecting blood (bodily fluid) from breast cancer patients for analyses (page 1063, col. 1, first paragraph), as stated in instant claim 4. Lehman et al. describe using paraffin-embedded tumor specimens and samples from patients undergoing drug treatments (page 1068, col. 1, third paragraph), as stated in instant claims 10 and 15.

Lehman et al. state the identification of woman at risk for development of breast cancer will have important implications for the prevention of cancers, treatment strategies, and

improved cure rates of these patients (page 1062, col. 2, third paragraph). Schraml et al. state their tissue microarray technology has the potential to greatly facilitate analysis of alterations in multiple tissue types (page 1966, col. 2, second paragraph). Schraml et al. state that tumor arrays are a powerful tool to rapidly screen different tumor types for gene copy number alterations (page 1966, col. 2, second paragraph). Schraml et al. state they have demonstrated the power of using minute arrayed tissue specimens for tumor screening (abstract). Lincoln et al. state bioinformatics includes methods to search databases quickly to analyze information and make predictions (col. 1, lines 31-37). Lincoln et al. state information manipulation has been made easier to perform and understand with the development of sophisticated computer database systems (col. 1, lines 62-64). It would have been obvious to one of ordinary skill in the art at the time the invention was made to make improvements to existing gene expression techniques tied to relational database systems, as stated by Lincoln et al, because even though these systems provide great power and flexibility in analyzing gene expression information, this technology is still in its infancy and further improvements are required to accelerate biological research for numerous applications (Lincoln et al. col. 2, lines 6-12). Therefore, it would have been obvious to one of ordinary skill in the art to improve efficiency of microarray analyses with minute frozen and bodily fluid samples from multiple cancer patients and multiple tumor types (as stated by Schraml et al. and Lehman et al.) and relaying such information of relational database systems (as stated by Lincoln et al.) in order to accelerate research and evaluation in therapeutic pharmaceutical development and other fields by providing broad amounts of important information to clients in an easy to perform and understand format, as stated by Lincoln et al. (col. 1, line 62 to col. 2, line 28).

Thus, Lincoln et al., in view of Schraml et al. and Lehman et al., motivate the instant claims.

It is reiterated that the phrases "for placement" on lines 2 and 3 as well as the phrase "wherein the profile array substrate allows testing... in the control oncology tissue microarray" in instant claim 1 are all intended uses which carry no patentable weight as to the article of manufacture being claimed. Applicant states that neither Lincoln et al., Schraml et al., nor Lehman et al. alone or in combination, teach, disclose, or suggest a control oncology tissue microarray comprising a normal tissue sample and samples representing cancer progression. This statement is found unpersuasive as the instant claims do not recite a microarray comprising a normal tissue sample, but rather a normal sample (see instant claim 1, line 5). Furthermore, samples of normal and cancerous types represent samples of cancer progression that is disclosed in the Lincoln et al. reference. Applicant states Lehman et al. do not teach a tissue microarray. It is noted that not every single reference in a 35 USC 103 (a) rejection needs to contain every single limitation found in the claims so long as the rejected limitations are found in at least one of the combination of references as well as a motivational statement for reasons to combine the references. Because all of the limitations of the instant invention are addressed in one of the three references and there is adequate motivation (i.e. improving efficiency) to combine the references, the references properly motivate the instant invention. Applicant's arguments are deemed unpersuasive for the reasons discussed above.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

January 11, 2005

Ardin H. Marschel 1/12/05
ARDIN H. MARSCHEL
PRIMARY EXAMINER